In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS
No. 18-22V
Filed: January 19, 2021
PUBLISHED

SUZANNE MULRENIN, on behalf of her minor child, R.M.,

Petitioner,

v.

SECRETARY OF HEALTH AND HUMAN SERVICES,

Respondent.

Special Master Horner

Decision Dismissing Petition; Influenza (Flu) Vaccine; Mast Cell Activation Syndrome (MCAS)

Andrew Donald Downing, Van Cott & Talamante, PLLC, Phoenix, AZ, for petitioner.
Darryl R. Wishard, U.S. Department of Justice, Washington, DC, for respondent.

DECISION[1]

On January 4, 2018, petitioner, Suzanne Mulrenin, filed a petition under the National Childhood Vaccine Injury Act, 42 U.S.C. § 300aa-10-34 (2012), alleging that her minor child, R.M., experienced post-vaccination symptoms later diagnosed as a Mast Cell Activation Syndrome ("MCAS"), caused or significantly aggravated by her November 16, 2015 influenza ("flu") vaccination. For the reasons set forth below, I conclude that petitioner is not entitled to an award of compensation. Upon my review, it is unlikely R.M. suffered MCAS or that MCAS would have been vaccine-caused if present.

I. Applicable Statutory Scheme

Under the National Vaccine Injury Compensation Program, compensation awards are made to individuals who have suffered injuries after receiving vaccines. In

[1] Because this decision contains a reasoned explanation for the special master's action in this case, it will be posted on the United States Court of Federal Claims' website in accordance with the E-Government Act of 2002. *See* 44 U.S.C. § 3501 note (2012) (Federal Management and Promotion of Electronic Government Services). **This means the decision will be available to anyone with access to the Internet.** In accordance with Vaccine Rule 18(b), petitioner has 14 days to identify and move to redact medical or other information the disclosure of which would constitute an unwarranted invasion of privacy. If the special master, upon review, agrees that the identified material fits within this definition, it will be redacted from public access.

general, to gain an award, a petitioner must make a number of factual demonstrations, including showing that an individual received a vaccination covered by the statute; received it in the United States; suffered a serious, long-standing injury; and has received no previous award or settlement on account of the injury. Finally – and the key question in most cases under the Program – the petitioner must also establish a *causal link* between the vaccination and the injury. In some cases, the petitioner may simply demonstrate the occurrence of what has been called a "Table Injury." That is, it may be shown that the vaccine recipient suffered an injury of the type enumerated in the "Vaccine Injury Table," corresponding to the vaccination in question, within an applicable time period following the vaccination also specified in the Table. If so, the Table Injury is presumed to have been caused by the vaccination, and the petitioner is automatically entitled to compensation, unless it is affirmatively shown that the injury was caused by some factor other than the vaccination. § 300aa-13(a)(1)(A); § 300 aa-11(c)(1)(C)(i); § 300aa-14(a); § 300aa-13(a)(1)(B).

In many cases, however, the vaccine recipient may have suffered an injury *not* of the type covered in the Vaccine Injury Table. In such instances, an alternative means exists to demonstrate entitlement to a Program award. That is, the petitioner may gain an award by showing that the recipient's injury was "caused-in-fact" by the vaccination in question. § 300aa-13(a)(1)(B); § 300aa-11(c)(1)(C)(ii). In such a situation, of course, the presumptions available under the Vaccine Injury Table are inoperative. The burden is on the petitioner to introduce evidence demonstrating that the vaccination actually caused the injury in question. *Althen v. Sec'y of Health & Human Servs.*, 418 F.3d 1274, 1278 (Fed. Cir. 2005); *Hines v. Sec'y of Health & Human Servs.*, 940 F.2d 1518, 1525 (Fed. Cir. 1991).

The showing of "causation-in-fact" must satisfy the "preponderance of the evidence" standard, the same standard ordinarily used in tort litigation. § 300aa-13(a)(1)(A); *see also Althen*, 418 F.3d at 1279; *Hines*, 940 F.2d at 1525. Under that standard, the petitioner must show that it is "more probable than not" that the vaccination was the cause of the injury. *Althen*, 418 F.3d at 1279. The petitioner need not show that the vaccination was the sole cause of the injury or condition, but must demonstrate that the vaccination was at least a "substantial factor" in causing the condition, and was a "but for" cause. *Shyface v. Sec'y of Health & Human Servs.*, 165 F.3d 1344, 1352 (Fed. Cir. 1999). Thus, the petitioner must supply "proof of a logical sequence of cause and effect showing that the vaccination was the reason for the injury;" the logical sequence must be supported by "reputable medical or scientific explanation, *i.e.*, evidence in the form of scientific studies or expert medical testimony." *Althen*, 418 F.3d at 1278; *Grant v. Sec'y of Health & Human Servs.*, 956 F.2d 1144, 1148 (Fed. Cir. 1992). A petitioner may not receive a Vaccine Program award based solely on his or her assertions; rather, the petition must be supported by either medical records or by the opinion of a competent physician. § 300aa-13(a)(1).

In what has become the predominant framing of this burden of proof, the *Althen* court described the "causation-in-fact" standard, as follows:

> Concisely stated, Althen's burden is to show by preponderant evidence that the vaccination brought about her injury by providing: (1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of proximate temporal relationship between vaccination and injury. If Althen satisfies this burden, she is "entitled to recover unless the [government] shows, also by a preponderance of the evidence, that the injury was in fact caused by factors unrelated to the vaccine."

Althen, 418 F.3d at 1278 (citations omitted). The *Althen* court noted that a petitioner need not necessarily supply evidence from medical literature supporting petitioner's causation contention, so long as the petitioner supplies the medical opinion of an expert. *Id*. at 1279-80. The court also indicated that, in finding causation, a Program fact-finder may rely upon "circumstantial evidence," which the court found to be consistent with the "system created by Congress, in which close calls regarding causation are resolved in favor of injured claimants." *Id*. at 1280.

Petitioner contends that the flu vaccine caused R.M.'s MCAS. Because MCAS is not listed on the Vaccine Injury Table, petitioner must satisfy the above-described *Althen* test for establishing causation-in-fact.[2]

II. Procedural History

Initially this case was assigned to Special Master Millman. (ECF No. 4.) Petitioner filed medical records marked as Exhibits 1-24. (ECF Nos. 6-9, 11.) On

[2] Although petitioner did initially plead both a cause-in-fact and significant aggravation claim, she presented this case as a cause-in-fact claim in her motion for a ruling on the record and urges a ruling in her favor based on the *Althen* test. (ECF No. 41.) I do note, however, that respondent observed in his recitation of facts that certain aspects of R.M.'s medical history, including prior allergies and treatment with cetirizine and montelukast, are potentially consistent with a pre-existing MCAS. (ECF No. 42, p. 4.) Nonetheless, respondent's position in this case is that R.M. never had MCAS. Additionally, although petitioner's expert noted the existence of pre-vaccination abdominal pain and allergic rhinitis, he described R.M. as "otherwise well" prior to vaccination and never attributed her pre-vaccination condition to MCAS. (Ex. 27; Ex. 37.) Rather, he opined that R.M.'s vaccination *led to the development* of symptoms consistent with MCAS. (Ex. 37, p. 2.) Accordingly, neither party has presented any theory of significant aggravation. In any event, the cause-in-fact and significant aggravation analyses overlap and the discussion below, regarding both R.M.'s diagnosis and petitioner's *Althen* presentation, would likewise preclude a significant aggravation claim related to R.M.'s alleged MCAS for all the same reasons. Where a petitioner in an off-Table case is seeking to prove that a vaccination aggravated a pre-existing condition, the petitioner must establish three additional factors. *See Loving v. Sec'y of Health & Human Servs.*, 86 Fed. Cl. 135, 144 (Fed. Cl. 2009) (combining the first three *Whitecotton* factors for claims regarding aggravation of a Table injury with the three *Althen* factors for off table injury claims to create a six-part test for off-Table aggravation claims); *see also W.C. v. Sec'y of Health & Human Servs.*, 704 F.3d 1352, 1357 (Fed. Cir. 2013) (applying the six-part *Loving* test.). The additional *Loving* factors require petitioners to demonstrate aggravation by showing: (1) the vaccinee's condition prior to the administration of the vaccine, (2) the vaccinee's current condition, and (3) whether the vaccinee's current condition constitutes a "significant aggravation" of the condition prior to the vaccination. *Id*.

February 22, 2018, Special Master Millman issued an order addressing her review of petitioner's medical records. (ECF No. 12.) She also attached an article regarding diagnostic criteria for MCAS marked as Court Exhibit 1. (*Id*. (citing Cem Akin, Peter Valent & Dean M. Metcalfe, *Mast Cell Activation Syndrome: Proposed Diagnostic Criteria*, 126 J. ALLERGY CLIN IMMUNOL 1099 (2010) (Court Exhibit 1).) Special Master Millman questioned the onset of petitioner's condition and the validity of urinalysis results upon which her doctor had relied. (ECF No. 12, pp. 2-3.)

Subsequently, petitioner filed additional medical records marked as Exhibit 25 and a statement of completion. (ECF Nos. 13-14.) She filed a response to Special Master Millman's February 22, 2018 Order on March 13, 2018. (ECF No. 15.) Following an initial status conference, petitioner filed further records marked as Exhibit 26 on May 14, 2017. (ECF No. 18.)

On May 17, 2018, respondent filed his Rule 4 report. (ECF No. 19.) Respondent recommended against compensation, contending that R.M.'s clinical history did not support a diagnosis of MCAS. Respondent also filed as two additional articles. (*Id*. at 17 (citing Cem Akin, *Mast Cell Activation Disorders*, 2 J ALLERGY CLIN IMMUNOL 252 (2014) (Ex. A); Cem Akin, *Mass Cell Disorders: An Overview*, UPTODATE, https://www.uptodate.com/contents/mast-cell-disorders-an-overview (last visited May 17, 2018) (Ex. B).) Respondent also contended that R.M.'s condition was better explained as Somatoform Symptom Disorder ("SSD"). (ECF No. 19, p. 17.)

Thereafter, petitioner filed an expert report by immunologist Jonathan Bernstein, M.D. (ECF No. 21; Ex. 27.) Respondent filed a responsive report by immunologist Andrew MacGinnitie, M.D. (ECF No. 24; Ex. C.) Petitioner subsequently filed further additional medical records. (ECF Nos. 27-28.)

This case was reassigned to me on June 5, 2019, and I held a status conference on November 18, 2019. Thereafter, each party filed a supplemental report by their respective experts. (ECF No 34; Ex. 37 and ECF No. 37; Ex. N.)

On April 8, 2020, petitioner advised in a status report that petitioner proposed to resolve the case through briefing and a decision on the written record. (ECF No. 38.) Respondent had no objection. (*Id*.) Petitioner filed a motion for a decision on the record on June 12, 2020. (ECF No. 41.) Respondent filed a response on July 31, 2020, and petitioner filed her reply on August 7, 2020 along with further updated records. (ECF Nos. 42-44.)

Accordingly, this case is now ripe for resolution. Although the suggestion of resolving this case on the written record arose from an agreement of the parties, I note that I have also separately determined that the parties have had a full and fair opportunity to present their cases and that it is appropriate to resolve this case without a hearing. *See* Vaccine Rule 8(d); Vaccine Rule 3(b)(2); *Kreizenbeck v. Sec'y of Health & Human Servs.*, 945 F.3d 1362, 1366 (Fed. Cir. 2020) (noting that "special masters must

determine that the record is comprehensive and fully developed before ruling on the record.").

III. Factual History

a. As Reflected in the Medical Records

R.M. was born on January 9, 2006. (Ex. 2, p. 1.) She received the flu vaccination at issue in this case on November 16, 2015, when she was nearly nine years old. (*Id*.) Prior to this vaccination she did have a history of stomachaches, allergies, and constipation. (Ex 9, p. 12; Ex. 21, pp. 108, 239; Ex. 26, pp. 14-23.) She has had a history of swollen throat, obstructive sleep apnea, tonsil-related issues, and tonsillar hypertrophy, which resulted in a tonsillectomy and adenoidectomy. (Ex. 18, p. 8, Ex. 19, p. 1, 5, 8.) Additionally, R.M. was admitted into urgent care on July 5, 2014 for a fever and sore throat. (Ex. 18, pp. 2-6.)

On November 5, 2012, at six years of age, R.M. was seen with reports of allergies and sniffles. (Ex. 26, p. 23.) She was reportedly taking Zyrtec and Singulair. (*Id*.) Respondent stresses that both of these medications can be used to treat MCAS. (ECF No. 42, p. 4.) By October of 2015, R.M.'s allergies were severe enough that she had begun immunotherapy (i.e. allergy shots). (Ex. 9, pp. 1-5.) Additionally, R.M. had a history of small lesion on her left ear that has been monitored from when she was five years old. (Ex. 13.)

R.M. also had pre-vaccination instances of abdominal pain beginning around age seven. On April 12, 2013, R.M. was seen for stomachache presenting with a sore throat. (Ex. 26, p. 20.) She was diagnosed with pharyngitis.[3] (*Id*.) About three months later on July 9, 2013, she was seen for abdominal pain with diarrhea, but not in the context of any apparent fever or illness. (Ex. 26, p. 19.) The following year she was seen again for abdominal pain with constipation on four occasions in April of 2014. (Ex. 26, pp. 14-17.)

R.M. saw Dr. Sheila Rao, her PCP, on April 15, 2015 for leg pain. (Ex. 3, p. 3.) Upon physical examination, Dr. Rao found tenderness in left hip, pain in lower gluteal region, and pain in upper hamstring. Additionally, there was also pain on palpation on her left knee and left ankle, and tenderness over left Achilles tendon. (*Id*. at 5.) Dr. Rao concluded right side patellofemoral stress syndrome, left side Achilles tendinitis and left hip pain. Dr. Rao ordered a hip x-ray and discussed relevant stretches to reduce pain or to elevate if pain persists. (*Id*.) R.M.'s hip x-ray was normal and revealed no osseous or articular abnormality. (*Id*. at 8.)

R.M. visited Dr. Rao again on November 16, 2015 with a chief complaint of ear pain. (Ex. 3, pp. 1-3.) She was assessed with serous otitis media and upper respiratory infection. R.M. had the flu shot at issue at this visit. (*Id*. at 3.)

[3] Pharyngitis means an "inflammation of the pharynx." (*Pharyngitis*, DORLAND'S MEDICAL DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=38409 (last visited on January 12, 2021)).

R.M. was seen at the emergency room on December 12, 2015 for generalized abdominal pain, where she was initially diagnosed and treated for pneumonia. (Ex. 3, pp. 155-56; Ex. 14, pp. 80, 89.) It was reported that R.M. presented to her pediatrician on December 4th and 5th for a low-grade fever, and on December 7, 2015,[4] R.M. started experiencing abdominal pain. (Ex. 3, p. 154.) Her urine culture indicated presence of Escherichia coli and pseudomonas aeruginosa. (*Id*. at 208; Ex. 14, p. 102, 116.) Her urine analysis tested positive for urobilinogen[5] and squam epithelial. (Ex. 14, p. 101.) However, her December 14, 2016 abdominal x-ray showed findings similar to her April 8, 2014 study and was otherwise normal. (Ex. 3, p. 11.) Her chest and cervical spine x-rays were also normal. (*Id*. at 12.) R.M. was discharged with pneumonia on the same day. (Ex. 14, pp. 80-82, 99.)

On December 18, 2015, R.M. presented to the emergency room again for continued abdominal pain and fatigue. (Ex. 3, p. 154.) Although her urinalysis was negative (possibly due to the antibiotics), R.M. was to continue her antibiotics for her presumed UTI. (*Id*. at 157.) Otherwise, the treating physician indicated unremarkable testing and suspected pneumonia. (*Id*.) On December 31, 2015, R.M. returned to the emergency room for persistent abdominal pain since December 7, 2015. (Ex. 3, p. 135.) "She originally did have some URI symptoms at the beginning of the illness when the pain started, but that has all resolved, but she continues to have the abdominal pain." (*Id*.) At this visit, R.M. denied vomiting, diarrhea, or urinary symptoms. R.M.'s repeated labs were again normal, with slightly elevated ALT, AST, and monocytes.[6] (*Id*. at 137.) R.M. was discharged home on the same day since her imaging were unremarkable. (*Id*. at 138.) Of note however, R.M.'s urine culture on January 2, 2016, indicated multiple organisms present, most likely due to contamination, and a repeat culture was suggested. (*Id*. at 148.)

R.M. had a follow up visit on January 5, 2016, regarding her chronic bilateral abdominal pain for "one and a half years."[7] (Ex. 3, p. 32.) R.M. was thought to have irritable bowel syndrome ("IBS"). (*Id*. at 35.) R.M. saw Dr. Marc L. Cullen on January 11, 2016 for abdominal pain lasting for one month. (Ex. 4, p. 1.) Upon review of multiple ultrasounds, x-rays, and lab reports, Dr. Cullen concluded that there's nothing to suggest a biliary or peptic etiology. On January 21, 2016, R.M. had a pelvis and abdomen MRI because of continued abdominal and pelvic pain. (Ex. 3, p. 10; Ex. 4, p.

[4] In another record, R.M. complained of continued abdominal pain and weakness since December 5, 2015. (Ex. 3, p. 11.)

[5] Urobilinogen is "a colorless compound formed in the intestines by the reduction of bilirubin. Some excreted in the feces, whereby oxidation it becomes urobilin, and some is reabsorbed and re-excreted either in the bile as bilirubin or in the urine, where is it later oxidized to urobilin." (*Urobilinogen*, DORLAND'S MEDICAL DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=52170 (last visited on January 12, 2021).)

[6] ALT and AST are liver enzymes and monocytes are white blood cells.

[7] This would place the onset of abdominal pain before the vaccination at issue.

5; Ex. 14, p. 10.) There was minimal fluid in the pelvic cavity, but the results were otherwise normal. (Ex. 4, p. 6; Ex. 14, p. 10.)

On February 1, 2016, R.M. visited Dr. Zachary Liss, urology specialist.[8] (Ex. 3, p. 31.) Upon physical examination, Dr. Liss reported R.M.'s abdomen to be soft, nontender, and nondistended. Additionally, there was no guarding, rebound, or abnormal peritoneal signs. (*Id*. at 31.) His impression was that R.M had nonspecific abdominal pain, but he doubted that her pain was genitourinary related. Dr. Liss planned to reevaluate R.M. in three months. (*Id*.)

Subsequently, on February 4, 2016, R.M. visited the pediatric gastrointestinal clinic at St. John Hospital and had a consultation with Dr. Hernando Lyons regarding her abdominal pain. (Ex. 3, p. 28-29.) Dr. Lyons indicated that R.M.'s lower abdominal pain began on December 7, 2015. (*Id*. at 29.) Dr. Lyons posited that R.M. chronic abdominal pain represented functional bowel disease and doubted that R.M. had inflammatory bowel disease. (*Id*. at 30-31.) However, her lab results suggested inflammatory bowel disease. (*Id*. at 16, 196.)

On February 27, 2016, R.M. visited the emergency department again for her chronic abdominal pain and headache. (Ex. 3, p. 125; Ex. 20, p. 3.) She was also noted to have a flushed face with swelling on her neck. (Ex. 20, p. 21.) Her urinalysis showed traces of ketones and blood, but was otherwise normal. (*Id*. at 28, 32.) R.M. received medication for her headaches and IV of fluids for concerns of possible abdominal migraines. R.M. was referred for a gastroenterology evaluation for chronic abdominal pain and echogenic hepatic parenchyma. (Ex. 3, pp. 125-26; Ex. 20, pp. 9-10.) Her labs were otherwise unremarkable. (Ex. 20, pp. 6-8.)

On March 7, 2016, R.M. had her first endocrinology evaluation with Dr. Delia M. Vazquez for concerns regarding her "development of hump on her back, abdominal pain, muscular weakness, and nausea." (Ex. 3, p. 118; Ex. 20, p. 51.) Since her evaluation did not reveal an etiology, Dr. Vazquez wanted repeated testing to explore a diagnosis of Cushing syndrome[9] and other hormonal dysfunction, specifically, a repeat 24-hour urine test for any signs of elevated cortisol levels. (Ex. 3, pp. 122-23.) The 24-hour urine test came back normal with no evidence of elevated cortisol secretion. (Ex. 20, p. 56.)

Thereafter, on March 10, 2016, R.M. had a gastroenterology evaluation with Drs. Andrew Singer and Frank W. DiPaola. (Ex. 3, pp. 111-16.) Dr. Singer recorded that R.M.'s abdominal pain first began in early December of 2015 and initially had a fever

[8] According to the handwritten records, R.M. continued seeking treatment from Dr. Liss regarding bladder problems and UTIs throughout 2016 and occasionally in 2017. (*See* Ex. 10.)

[9] Cushing syndrome, which is also known as Cushing disease is "a complex of symptoms caused by hyperadrenocorticism due either to a neoplasm of the adrenal cortex or adenohypophysis, or to excessive intake of glucocorticoids. Symptoms may include adiposity of the face, neck, and trunk…." (*Cushing syndrome*, DORLAND'S MEDICAL DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=110487 (last visited on January 12, 2021).)

upon onset, which was later attributed to her UTI. Additionally, R.M. reported that her abdominal pain persisted since onset and described the pain as constant, nonstop, and present daily. R.M. also reported constant nausea, but no vomiting. R.M. has been treated with Levsin in case of an underlying GI disease, but without relief. (*Id*. at 111-12.) R.M.'s abdominal ultrasound, obtained on February 27, 2016, revealed no abdominal ascites, but an echogenic liver that is compatible with diffuse hepatocellular dysfunction. (*Id*. at 115.) Dr. Singer agreed that an evaluation for Cushing syndrome is warranted as abdominal pain is seen in patients with Cushing disease. (*Id*.) However, R.M.'s urine analysis showed normal urine free cortisol and suppressed serum cortisol, not supportive of Cushing syndrome. (Ex. 20, p. 91.) Additionally, Dr. Singer agreed with the previous pediatric GI evaluators that there is no underlying GI disease and unless R.M.'s endocrine evaluation indicate otherwise, Dr. Singer recommended treatment for functional abdominal pain, such as medication and psychology referral. (Ex. 3, pp. 115-16.) R.M.'s urinary test retrieved on March 10, 2016 indicated findings consistent of adrenal insufficiency but was otherwise normal.[10] (Ex. 14, p. 34.)

On March 28, 2016, R.M. was evaluated by Dr. Ram Menon for a second opinion at the Pediatric Endocrine Clinic. (Ex. 3, p. 97-101.) Dr. Menon recorded that R.M. has had several referrals including "1) GI referral (Feb 4th) – no pathology found but elevation of lipase enzyme; 2) Urology (Feb 1) due to 2 UTIs (culture positive without symptoms – but polyuria) treated with antibiotics; 3) General Surgery – Jan 11, 2016 – abdominal MRI was negative. As noted [] pending referral to Rheumatology." (*Id*. at 98.) R.M.'s 24-hour urine free cortisol (UFC) test results, taken on March 10, 2016, were normal and thus, not supportive of Cushing syndrome. (*Id*. at 100, 108.) Dr. Menon did not find any endocrinal etiology of R.M.'s syndrome and referred her to neurology instead. (*Id*. at 101.)

R.M. had an initial consultation with Dr. Allison Effron and Dr. Erin Elizabeth Neil Knierbein on March 31, 2016 regarding her ongoing symptoms, including daily headache and change in gait. (Ex. 3, p. 179-83.) It was noted that R.M. started with abdominal pain and nausea in December 2015 and in January 2016, she began having pain with ambulation. (*Id*.) Due to the difficulty walking, petitioner had a wheelchair for R.M. for leaving the house. (*Id*. at 180.) Dr. Effron summarized her overall findings:

> She has now a 4 month history of symptoms that began with abdominal pain and nausea, and now includes persistent daily headaches, abnormal gait without weakness, episodic blurry vision, and weight gain. She has seen by GI (multiple providers), endocrinology, ophthalmology, and has an appointment with rheumatology later this week. Work-up thus far has been unrevealing. Her symptoms do not fit with a clear organic etiology at this time.

[10] R.M.'s urine chemistry report from February 11, 2016 also yielded similar interpretations. (Ex. 14, p. 44.)

(Ex. 3, p. 182.) Overall, Dr. Effron was concerned about a somatic symptom disorder.[11] (*Id*. at 183.)

On April 1, 2016, petitioner had a rheumatology consultation with Drs. Anjali S. Sura and Meredith P. Riebschleger. (Ex. 20, p. 108.) Upon review of R.M.'s medical records, laboratory workups, and physical examination, Dr. Sura indicated that R.M. did not appear to have any rheumatic disorder. Dr. Sura brought up the possibility of a conversion disorder and encouraged R.M. to see a pain psychologist. (*Id*. at 111.)

R.M. also saw Dr. Iqbal Allarakhia for a neurology evaluation on April 12, 2016 and reported experiencing symptoms of nausea, lower abdominal pain ("occurring frequently"), and weight gain since the end of last November, headaches that abruptly started in February, and difficulty walking[12] that started within the last few weeks. (Ex. 3, pp. 85-88.) It was noted that R.M. has been using a wheelchair[13] to get around although she is able to walk short distances. (*Id*. at 88.) Due to the excessive weight gain, the hump on R.M.'s back, and increased hair growth, Dr. Allarakhia suspected a possible underlying endocrinologic dysfunction regarding her gait abnormality. On the same day, R.M. saw Dr. Anne Premchand for management of her hyper-triglycerides. (Ex. 3, pp. 175-77.)

Dr. Peter M. Gerrits evaluated R.M. on April 18, 2016 for Cushing disease. (Ex. 3, p. 167; Ex. 15, p. 18.) Dr. Gerrits reported that Cushing syndrome was ruled out with the standard 24-hour urines and dexamethasone suppression testing and that additional endocrine testing was not warranted. He also agreed that psychological counseling is recommended. (Ex. 3, p. 170.) Additionally, Dr. Paul Padesky, her PCP, evaluated R.M. on April 22, 2016, regarding frequent urinary problems and assessed her with an acute UTI. (*Id*. at 80-84.) Dr. Padesky noted that R.M. have had two previous endocrinology evaluations, both evaluations recommended a follow up psych evaluation. (*Id*. at 83.) Moreover, her urinalysis results were negative. (*Id*. at 84.)

On April 26, 2016, R.M. presented to the emergency department for ongoing lower abdominal pain and worsening gait instability. (Ex. 3, pp. 91, 95; Ex. 20, p. 140.) R.M. reported that the abdominal pain and nausea are consistent with her previous complaints and denied experiencing vomiting or diarrhea. (Ex. 3, p. 92.) Her urinalysis revealed abnormal results, but for the traces of blood and red blood cells. (*Id*. at 95.) Upon evaluation, the treating physicians were concerned about a possible somatoform

[11] Somatoform disorder is "a group of disorders in which physical symptoms suggesting physical disorders for which there are no demonstrable organic findings or known physiologic mechanisms, and for which there is positive evidence, or a strong presumption that the symptoms are linked to psychological factors; *e.g.,* hysteria, conversion disorder, hypochondriasis, pain disorder, somatization disorder, body dysmorphic disorder, and Briquet syndrome." (*Somatoform disorder*, STEDMANS MEDICAL DICTIONARY, at 260650.)

[12] According to the record as a whole, R.M. started experiencing difficulty walking in January 2016. (Ex. 3, pp. 179-80.)

[13] Petitioner averred in her affidavit that R.M. was confined to a wheelchair for over a year starting in February 2016. (Ex. 1, p. 2.)

or conversion disorder. (*Id*. at 95.) R.M. was admitted for somatoform disorder. During her stay, R.M. had a pediatric psychology consult with Dr. Kristin Ann Kullgren to "address multiple somatic complaints including headache, gait disturbance, headache, stomach ache, and nausea leading to significant functional impairment over the past several months," that her family indicated started two weeks after her flu shot. (Ex. 20, p. 159.) Dr. Kullgren diagnosed R.M. with somatic symptom disorder ("SSD") and recommended intervention, specifically for inpatient rehabilitation. (*Id*.) Additionally, R.M. was seen by Dr. Nasuh M. Malas for a consultation for somatic symptom disorder and Dr. Malas agreed that R.M.'s clinical symptoms were consistent with SSD. (*Id*. at 163, 167.) R.M. was discharged on April 28, 2016 with orders for follow-up physical therapy and further psych evaluation. (Ex. 3, pp. 78, 96.)

Following her visit to the hospital, R.M. had a follow up exam on May 3, 2016 with Dr. Rao, who maintained somatoform disorder was the diagnosis. (Ex. 3, pp. 78-79.) At this visit, R.M. herself reported worsening symptoms of abdominal pain and difficulty walking since discharge. (*Id*. at 78.) R.M. started outpatient physical therapy in May of 2016 for her gait dysfunction. (Ex. 5, p. 41.)

On May 5, 2016, R.M. sought primary care from Dr. Jeffrey J. Fisher. (Ex. 5, p. 1.) R.M.'s history indicated that "[s]he started having abdominal pain and felt nauseous a few days after [s]he received flu shot 11/16/15. It all seemed to start with stomach pain and has persisted." (*Id*.) Additionally, R.M. experienced leg weakness and has a history of UTI and somatoform symptom disorder. (*Id*.) Dr. Fisher assessed R.M. with joint pain, facial rash, weakness, and ordered a brain MRI and EMG. R.M.'s labs results showed positive for anti-nuclear antibody ("ANA") and elevated protein and insulin levels. (*Id*. at 5-6.) About a week later, R.M. returned to Dr. Fisher with complaints of urine pain. (*Id*. at 20.) R.M. was diagnosed with a UTI. (*Id*. at 23.) Although her urinalysis was negative, R.M.'s urine culture detected Citrobacter freundii complex. (*Id*. at 16; Ex. 16, p. 12.) Also, her abdomen ultrasound revealed heterogenous texture of the liver with echogenic areas that are suggestive of fatty infiltration. (Ex. 5, p. 17.) Additionally, R.M. saw Dr. Fisher for a rash on June 3, 2016, which Dr. Fisher attributed due to a drug eruption/allergic reaction. (*Id*. at 24-25.) However, the following day, R.M. went to the emergency room for the allergic reaction and shortness of breath. (*Id*. at 27; Ex. 17, p. 8.) She was discharged on the same day. (Ex. 17, p. 10.)

On June 14, 2016, R.M. was evaluated by Dr. Eileen M. McCormick at the Beaumont Children's neurology clinic. (Ex. 8, p. 11; Ex. 15, p. 13.) This presents R.M.'s third neurological opinion. Upon review of the prior medical records and assessment, Dr. McCormick's impression was that R.M. had "several month duration of alleged gait abnormality with early morning headaches that are not characteristic of migraine currently. Also lower abdominal pain, frequent nausea, and recurrent UTIs." (Ex. 8, p. 13.) Dr. McCormick indicated that R.M.'s physical therapy performance has been inconsistent. She also noted that the R.M.'s complaints began after flu vaccination and viral illness, but did indicate that the symptoms were not characteristics of Guillain-Barre syndrome or chronic inflammatory demyelinating polyneuropathy. (*Id*.

at 14.) Per Dr. McCormick's order for upper and lower extremities somatosensory evoked potentials testing, R.M.'s results were normal. (*Id*. at 18.)

R.M. visited Dr. Edward Dabrowski regarding her difficulty walking on June 17, 2016. (Ex. 7, p. 19.) His first impression was that R.M. had a progressive gait disorder, pain of unclear etiology that may involve her central nervous system and somatic disorder. (*Id*. at 21.) Dr. Dabrowski agreed with the somatic/conversion disorder diagnosis upon review of the hospitalization records and indicated that R.M.'s physical exam "is not consistent for ataxia throughout motor movements or uniform neurological deficits." (*Id*. at 16.) Dr. Dabrowski noted that R.M.'s "ability to ambulate has gotten progressively worse and patient now utilizes a wheelchair." (*Id*. at 19.) On June 23, 2016, R.M. presented to Grosse Pointe Beaumont Hospital for gait disturbance, headache, recurrent UTIs, and bladder incontinence. (Ex. 17, p. 15.) Her MRIs were unremarkable. (*Id*. at 32-41.) Her abdomen ultrasound showed heterogenous texture of the liver that suggested fatty infiltration. (*Id*. at 41.) She was discharged on the same day. (*Id*. at 21, 54.)

Following urodynamic testing, R.M. visited Dr. Dabrowski again on September 28, 2016. (Ex. 7, p. 7.) Dr. Dabrowski suggested that R.M. has a mitochondrial disorder, but also considered a psychogenic component, although "this does not explain the bladder complaints." (*Id*. at 9.) On December 30, 2016, R.M. had another visit for management of her gait disturbance. (*Id*. at p. 1.) R.M. has been in physical therapy and was transitioning better with her wheelchair. Additionally, R.M. continued having persistent abdominal pain. (*Id*.) Dr. Dabrowski reported improvement regarding her gait disturbance and remained that a "psychogenic component possibility. However, this does not explain the bladder complaints." (*Id*. at 3.)

On July 25, 2016, R.M. had another neurology evaluation with Dr. McCormick. (Ex. 8, p. 6; Ex. 15, p. 8.) Dr. McCormick strongly recommended psychiatry evaluation and counseling for possible somatoform/conversion disorder. However, because conversion disorder is a diagnosis of exclusion, Dr. McCormick wanted additional testing. (Ex. 8, p. 8.) On August 11, 2016, R.M. had a neuro-interventional radiology consultation and a lumbar puncture and CSF study was ordered. (Ex. 5, pp. 55, 57; Ex. 16, p. 107.) Petitioner reported a history of gradual progression of abdominal pain, gait abnormality, headaches, joint pains, UTI's, and back pain. (Ex. 5, p. 55.) Dr. McCormick noted that R.M. uses a wheelchair for her muscle weakness. (*Id*.)

On August 29, 2016, R.M. returned to Dr. Fisher for left hip pain; however, imaging did not identify any abnormality. (Ex. 5, pp. 60, 64.) However, Dr. Fisher noted in a subsequent visit that R.M. was still confined to a wheelchair due to her muscle weakness, but physical therapy has shown improvement. (*Id*. at 69.)

On November 14, 2016, R.M. had a re-evaluation with Dr. McCormick following her spinal tap and CSF (cerebrospinal fluid) analysis, which were normal. (Ex. 8, p. 1; Ex. 15, p. 1.) R.M. complained that she experienced "tummy aches that 'never goes away.'" (Ex. 8, p. 1.) Dr. McCormick noted that R.M.'s urodynamics documented

inappropriate bladder emptying and a tendency of urine retention. (Ex. 15, p. 1.) Additionally, her test results, including from her spinal tap, were normal except for elevated liver enzymes. (*Id*.) Dr. McCormick brought up the possibility of somatoform/conversion disorder again and recommended repeat spinal tap, EMG, and skin biopsy. Additionally, "[i]t may indeed be helpful to document small fiber involvement given her GI symptoms and alleged sensory symptoms." (Ex. 8, p. 4.) R.M. continued experiencing abdominal pain and weakness throughout the remaining year. (Ex. 5, pp. 65, 69.)

On January 18, 2017, R.M. had an initial physical therapy examination for her difficulty with walking at Neil King Physical Therapy – St. Clair Shores. (Ex. 5, p. 85; Ex. 11, p. 1.) Regarding her mobility issue, it was noted that R.M. was able to use assistive devices, including scooter and wheelchair, in order to aid with ambulating. (Ex. 11, p. 1.) Petitioner indicated that R.M. previously had physical therapy from April 2016 to December 2016 at St. John's. (Ex. 11, p. 87.) It was noted that her rehabilitation potential was fair "due to non-specific diagnoses and extensive diagnostic testing without a clear picture of cause for inability to walk." (Ex. 11, p. 3.) Her treatment was for twice a week for eight weeks. (*Id*. at 4.) At her sessions, R.M. still complained of bad headaches and indicated no change in daily abdominal pain. (*See e.g.*, *Id*. at 11, 16, 19, 26.) However, R.M. had improvements regarding her walking since starting physical therapy. (*Id*. at 37, 40, 47.) On May 9, 2017, R.M. had a recertification evaluation, at which petitioner reported that R.M. has small fiber neuropathy and a mast cell test was performed to rule out any autonomic dysfunction. (*Id*. at 57.) However, R.M. missed a couple of sessions in June and petitioner reported that in July, R.M. sprained her ankle. (*Id*. at 79-84.)

Throughout 2017, R.M. continued to have abdominal pain, however she also had persistent respiratory symptoms, namely congestion, for two months. (Ex. 5, p. 75, 87, 103.) R.M. was also assessed with another UTI, abdominal pain, and weakness. (*Id*. at 79.) Specifically, on March 24, 2017, R.M. reported five days of moderate and intermittent abdominal pain and nausea. (*Id*. at 87.) Thereafter, on March 30, 2017,[14] R.M. went to the emergency center regarding her lower abdominal pain. At this visit, petitioner "relates that [R.M.] has experienced a reaction to the flu vaccine the year prior which had left [R.M.] unable to walk until recently," while R.M. indicated that the pain spans across her lower abdomen. (*Id*. at 95.)

Also, starting in 2017, R.M. was treated at Mayo Clinic. (Ex. 12.) She was evaluated by multiple specialists and undergone multiple testing for her various symptoms, including urology, dermatology, and endocrinology. (*Id*. at 30, 51, 53.) R.M. was referred to Dr. Jeanne Tung for abdominal pain and was seen on April 12, 2017. (*Id*. at 42.) Dr. Tung recorded that R.M. was "overall healthy until receiving an influenza vaccine in November 2015. She tolerated prior vaccines well. She then began having

[14] There are also records indicating R.M. was at Grosse Pointe Beaumont Hospital on March 29, 2017 for lower abdominal pain. (Ex. 17.) She was there from about 5:00pm and was discharged later in the evening after 10:00pm since she was feeling better. (*Id*. at 6.)

diffuse abdominal pain (worse in the epigastrium[15] and lower abdomen), which led to the point of difficulty with walking." (*Id*.) Dr. Tung indicated that the GI pain and the difficulty walking were unlikely to be related and inflammatory bowel disease was also unlikely. (*Id*. at 43.) Dr. Tung wanted to look for evidence of mast cell disorder and microscopic colitis. (*Id*.) Additionally, on the same day, R.M. saw Dr. Joline E. Brandenburg to evaluate for her rehabilitation needs. (*Id*. at 45.) Dr. Brandenburg concluded that there was not a unifying etiology to explain R.M.'s multiple symptoms, but they were suggestive of an autonomic dysfunction and/or small fiber neuropathy. (*Id*. at 47.)

R.M. was treated by Dr. Douglas A. Husmann for urinary incontinence and recurrent URI. (*Id*. at 30, 55.) Dr. Husmann indicated that urodynamic studies showed that R.M. has an overactive bladder and the uroflow studies were within normal limits. He diagnosed her with voiding dysfunction, recurrent urinary tract infections, and POT syndrome, noting that "[f]rom a urologic standpoint, [R.M.] has had significant improvement in her voiding habits just with time. At this point, we would recommend that she be on a timed-voiding interval urinating every two hours while awake along with maintenance of a voiding calendar." (*Id*. at 31.) Otherwise, no other intervention was necessary. (*Id*.)

R.M. saw Dr. Kelsey M. Klaas for an evaluation for abdominal pain, flushing, palpitations, and fatigue. (*Id*. at 23, 62.) Dr. Klaas indicated that R.M. had recently undergone a colonoscopy and upper endoscopy, which yielded normal results. (*Id*. at 23-24, 33.) Upon physical examination, Dr. Klaas noted that R.M.'s gait was now normal and determined that R.M. meets the criteria for Tourette's syndrome. (*Id*. at 26, 29.) R.M. returned later to review test results. (*Id*. at 23, 25.) Additionally, Dr. Klaas noted that testing for mast cell mediators in the absence of symptoms would often turn out negative. (*Id*. at 23.) Dr. Klaas also ruled out Cushing disease as a result of her normal cortisol levels and because R.M.'s symptoms have been suspicious for small fiber neuropathy. Dr. Klaas wanted her to begin a trial of gabapentin[16] even though her vitamin B12 levels were normal and sweat tests were outstanding. (*Id*. at 24.) R.M.'s transaminases levels were elevated, suggestive of fatty liver disease. (*Id*.)

Like Dr. Klaas, Dr. Tung gave a report following R.M.'s lab work performed on April 25, 2017, indicating that R.M.'s liver tests were elevated, and her cholesterol profile was abnormal. (*Id*. at 17.) Based on these results, Dr. Tung wanted to test for a specific metabolic disorder and have R.M. see a liver specialist, although Dr. Tung did not think the abnormal liver tests and high cholesterol would explain R.M.'s pain and flushing. (*Id*.) On May 9, 2017, Dr. Klaas reported that R.M.'s lab results indicated elevated levels of "2,3-dinor 11b Prostaglandin F2a" that raised concerns for mast cell

[15] Epigastrium is "the upper middle region of the abdomen, located within the infrasternal angle, superior to the subcostal plane." (*Epigastrium*, DORLAND'S MEDICAL DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=16844 (last visited on January 12, 2021).)

[16] Gabapentin is an anticonvulsant that is used as treatment for partial seizures and management for postherpetic neuralgia. (*Gabapentin*, DORLAND'S MEDICAL DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=19523 (last visited on January 12, 2021).)

problems. (Ex. 12, pp. 6, 14.) However, Dr. Klaas noted that other markers indicative of mast cell disorder, tryptase, N-Methylhistamine, and Leukotriene E4, were all normal. (*Id*.) Dr. Klaas recommended further follow up with an allergist. (*Id*. at 14.)

R.M. was further evaluated by Dr. Devang Doshi as a new patient for evaluation of mast cell disorder on June 9, 2017. (Ex. 6, pp. 22-23.) After reviewing R.M.'s most recent workup which he indicated revealed elevated F2 results per 24-hour urinalysis, Dr. Doshi was "inclined to believe that she does have a mast cell disorder." (*Id*. at 3, 24.) For further confirmation, Dr. Doshi recommended various testing including biopsies and additional blood work. (*Id*. at 3.) Dr. Doshi started R.M. on various medications including Allegra, Zantac, Singular, and Cromolyn. (*Id*. at 3-4.) However, in a letter from Dr. Tung from the Mayo Clinic Pediatric Gastroenterology, dated June 19, 2017, it was revealed that an additional staining for mast cells was performed in R.M.'s GI samples and the staining was negative. (Ex. 12, p. 10.) An addendum was added to R.M.'s general biopsy indicating that the stains show normal numbers of mast cells. (*Id*. at 80.)

During R.M.'s well child visit with Dr. Fisher on August 15, 2017, Dr. Fisher indicated that R.M. was diagnosed with mast cell activation syndrome and was being treated by Dr. Doshi. (Ex. 5, p. 110.) Dr. Fisher included MCAS as an assessment following this visit. (*Id*. at 113.) Additionally, Dr. Fisher noted that he advised various vaccinations for R.M., however, "parents refuse due to concern for ongoing mast cell activation syndrome – they wish to discuss with Dr. Doshi (Allergist)." (*Id*. at 114.) R.M. saw Dr. Doshi again on August 24, 2017 for a follow up visit regarding her mast cell disorder. (Ex. 6, p. 17.) During this visit, R.M. complained of abdominal pain, heat sensitivity, joint pain, and difficulty sleeping, although her headaches were less frequent. (*Id*.) Dr. Doshi recommended a low histamine diet and to continue with physical therapy. (Ex. 6, p. 29.)

On October 3, 2017, R.M. presented to Dr. Fisher with symptoms "compatible with acute gastroenteritis. She has had recent onset of nausea and diarrhea."[17] (Ex. 5, p. 115.) Dr. Fisher assessed R.M. with abdominal pain and gastroenteritis and ordered R.M. to follow up with Dr. Doshi for mast cell problem. (*Id*. at 117.) A couple of days later, R.M. went to the emergency room for generalized body aches. (*Id*. at 124.) As part of her history of present illness, R.M. was reported to have a prior history of mast cell disorder and that her chronic symptoms of malaise, fatigue, myalgias, and joint pain worsened over the past one and a half weeks. (*Id*.) The treating physician indicated that R.M. has mast cell degranulation disorder, chronic abdominal pain, urinary retention, and chronic dysuria and was sent to the ER by PCP for "'dehydration workup.'" (*Id*.) Her lab results indicate a presence of EBV-VCA, suggestive of a primary infection. (Ex. 16, p. 286.) R.M. was discharged home with a diagnosis of fatigue and malaise (possible viral syndrome), after receiving IV fluids. (Ex. 5, pp. 124,

[17] Dr. Fisher noted conflicting remarks regarding abdominal pain, where the chief complaint was presented as abdominal pain and that R.M. had nausea, abdominal pain, and joint pain for one week. However, in the same section under history of present illness, Dr. Fisher also noted no significant abdominal pain. (Ex. 5, p. 115.)

128.) However, a couple of days later on October 7, 2017, R.M. returned to the emergency room, but was discharged on the same day. (Ex. 16, p. 303-06; Ex. 23, p. 7.)

Thereafter, R.M. saw Dr. Doshi again on October 18, 2017 for ongoing care of her mast cell disorder. (Ex. 22.) Dr. Doshi indicated that "[g]iven the overall improvement in her constitutional symptoms with the use of antihistamines, ketotifen, and cromolyn, I feel her symptoms most likely fit with a clinical diagnosis of mast cell disorder." (*Id*. at 4.) He also recommended that R.M. continue receiving her annual flu vaccination. (*Id*. at 5.)

In 2018, R.M. sought care from Dr. Ayesha Fatima for chronic abdominal pain at the Pediatric GI clinic. (Ex. 25.) Dr. Fatima indicated that R.M. had a history of mast cell disorder. (*Id*. at 4.) R.M. was recommended a low FODMAP diet and probiotics. She was diagnosed with chronic abdominal pain and chronic nausea. (*Id*.) According to her records, R.M. still experienced abdominal pain in 2019 and sought treatment from Dr. Doshi for her mast cell disorder. (Ex. 45, pp. 6-7.)

b. As Reflected in Petitioner's Affidavit

Ms. Mulrenin indicated that prior to the vaccination at issue in this case, R.M. was a healthy and active girl, active in school and several sports. (Ex. 1, p. 1.) At the time of her November 16, 2015 flu vaccination, R.M. had an upper respiratory infection and an ear infection. (*Id*.) Beginning the next day, she began experiencing abdominal pain that "has been a constant in her life since the vaccination." (*Id*.)

Although she did not specify the onset, she also described additional symptoms as follows: "weakness in her upper and lower extremities and a very unstable gait. She also has flushing of her face that comes and goes, constant nausea, tics, blurred vision that comes and goes, headaches every morning and a hard time getting to sleep at night. R.M. has rashes and hives, muscle spasms, blurred vision, light and sound sensitivity, difficulty concentrating, hands and feet that have a severe burning feeling that comes and goes, tachycardia and shortness of breath." (*Id*.)

Ms. Mulrenin described R.M. as "walking slower and slower each day" during her fourth-grade year, often unable to keep up with her class. (*Id*. at 2.) She would often be taken home from school early, flushed and complaining of stomach pain. (*Id*.) Ms. Mulrenin indicated that beginning in February of 2016, R.M. began using a wheelchair and a walker. (*Id*.) She used the wheelchair for about a year. (*Id*.) During this time, R.M. could not attend school and did homework at home. (*Id.* at 2-3.)

Ms. Mulrenin also described a noticeable decline in R.M.'s gait and ability to be upright in April of 2016. (*Id*.) She indicated that at this time R.M. was admitted to Mott's Children's Hospital where she received a diagnosis of Somatic Symptom Disorder, which Ms. Mulrenin felt confident was not correct. (*Id*. at 2-3.) After changing insurance

in January of 2017, R.M. was able to be seen at the Mayo Clinic and ultimately by Dr. Doshi. (*Id*. at 3.)

IV. Summary of Expert Opinions and Qualifications

a. Petitioner's Expert - Dr. Jonathan Bernstein

Johnathan Bernstein, M.D., is a Professor of Clinical Medicine within the immunology division of the Department of Internal Medicine at the University of Cincinnati College of Medicine as well as the Director of Clinical Research at the school's Immunology Research Center. (Ex. 28, pp. 1, 6.) He is also a partner with the Bernstein Allergy Group and Clinical Research Center. (*Id*.) Dr. Bernstein earned his medical degree at the University of Cincinnati College of Medicine in 1985. (*Id*.) He completed a two-year fellowship in allergy and immunology in 1990 at Northwestern University in Chicago, Illinois. (*Id*.) He is board certified in internal medicine and pediatrics and a diplomate of the American Board of Allergy and Immunology. (*Id*. at 2.) His curriculum vitae lists numerous research grants and publications.

Dr. Bernstein endorsed Dr. Doshi's diagnosis of MCAS. (Ex. 27, p. 2.) He explained that MCAS has a heterogeneous clinical presentation from one patient to the next and opined that R.M. has many of the relevant clinical symptoms. (*Id*.) He indicated that, where primary and secondary disorders of mast cell activation have been ruled out, MCAS diagnostic criteria includes episodic symptoms affecting two or more organ systems, symptom response to certain treatments, and elevated urinary or serum markers. (*Id*. at 3 (Table 1).) Dr. Bernstein also stressed that no other plausible diagnosis is available. (*Id*. at 2.)

Dr. Bernstein further opined that R.M. experienced a progressive worsening of her symptoms that was in temporal proximity of and causally related to her Fluzone vaccination. (*Id*.) Based on prior articles suggesting a role for tetanus toxoid vaccination in the development of allergic disease, Dr. Bernstein hypothesized that mast cell activation can develop after vaccination generally. He described "a scenario where the production of IgG autoantibodies actively generated by influenza vaccination as seen with other vaccines such as tetanus could induce both mediator release from activated mast cells and Th2 cytokine production resulting in MCAS." (*Id*.)

In his supplemental report, Dr. Bernstein additionally cited publications which he indicated support a relationship between influenza A and mast cell activation in both human and mouse studies. (Ex. 37, p. 2.) He opined that "[t]hese data collectively support the direct relationship between R.M.'s vaccination with influenza A and the development of symptoms consistent with MCAS." (*Id*.)

b. Respondent's Expert - Dr. Andrew MacGinnitie

Dr. MacGinnitie currently serves as an attending physician and clinical director for the Division of Immunology at Boston Children's Hospital. (Ex. D, p. 2.) Additionally,

he is an associate professor at Harvard Medical School. (*Id*. at 1.) Dr. MacGinnitie received his medical degree and doctorate degree in pathology from the University of Chicago Pritzker School of Medicine. (*Id*. at 1.) From 1998 to 2004 he completed combined residency in pediatrics and fellowship in allergy and immunology at Children's Hospital. (*Id*.) He is board certified in allergy/immunology and pediatrics. (*Id*.) Like Dr. Bernstein, he lists a number of research grants and publications on his curriculum vitae.

Dr. MacGinnitie disagrees that MCAS is the correct diagnosis for R.M. (Ex. C, p. 4.) Applying the same diagnostic criteria cited by Dr. Bernstein, he stresses that R.M.'s symptoms were not episodic and that her primary presentation of abdominal pain is not typical of MCAS. (*Id*.) He also disagrees that R.M.'s elevated urinary marker satisfies the diagnostic criteria. Specifically, he indicates that she had elevated markers after only a single random urine sample whereas the diagnostic criteria require elevation on a 24-hour urine sample. (*Id*. at 5; Ex. N, p. 2.) Dr. MacGinnitie also noted that R.M. had additional symptoms not associated with MCAS (such as weakness and urinary retention) and stressed that MCAS is over diagnosed. (Ex. C, pp. 4-5.) To the extent Dr. Bernstein discussed dysautonomia, Dr. MacGinnitie disagreed that R.M. suffered dysautonomia and that dysautonomia is associated with MCAS. (Ex. N, p. 1.)

Even if R.M. did have MCAS, Dr. MacGinnitie also disagrees that there is reliable evidence that a flu vaccine can cause the condition. (Ex. C, pp. 6-7; Ex. N, p. 2.) He also opines that R.M.'s own clinical course is inconsistent with vaccine causation both because she tolerated prior flu vaccines well and because she had certain relevant symptoms prior to the vaccination at issue. (Ex. C, pp. 6-7.) He also noted that none of her treating physicians opined that her condition was vaccine-caused. (*Id*. at 6.)

V. Findings of Fact – R.M. Did Not Suffer MCAS

In this case, R.M. has a fairly complicated medical history and her correct diagnosis is disputed. When faced with disagreement among qualified experts regarding the identification and nature of a disputed injury, the Federal Circuit has concluded that it is "appropriate for the special master to first determine what injury, if any, [is] supported by the evidence presented in the record before applying the *Althen* test to determine causation." *Lombardi v. Sec'y of Health & Human Servs*., 656 F.3d 1343, 1351-53 (Fed. Cir. 2011). Importantly, however,"[t]he function of a special master is not to 'diagnose' vaccine-related injuries, but instead to determine 'based on the record as a whole and the totality of the case, whether it has been shown by a preponderance of the evidence that a vaccine caused the [petitioner]'s injury.'" *Andreu v. Sec'y of Health & Human Servs*., 569 F.3d 1367, 1382 (Fed. Cir. 2009) (quoting *Knudsen v. Sec'y of Health & Human Servs.*, 35 F.3d 543, 549 (Fed. Cir. 1994)).

Nonetheless, petitioner must "specify [her] vaccine-related injury and shoulder the burden of proof on causation." *Broekelschen v. Sec'y of Health & Human Servs*., 618 F.3d 1339, 1346 (Fed. Cir. 2010). "Although the Vaccine Act does not require absolute precision, it does require the petitioner to establish an injury – the Act specifically creates a claim for compensation for 'vaccine-related injury or death.'" *Stillwell v. Sec'y of Health & Human Servs*., 118 Fed. Cl. 47, 56 (2014) (quoting

42.U.S.C. § 300aa-11(c)). And, in any event, a petitioner must prove by a preponderance of the evidence the factual circumstances surrounding her claim. § 300aa–13(a)(1)(A). In this case, petitioner has premised her causation-in-fact analysis on her allegation that she suffers MCAS. (ECF No. 41, p. 24.) Accordingly, before reaching an *Althen* analysis, a threshold question is whether R.M. actually suffered MCAS as alleged. For the reasons discussed below, I conclude that she did not suffer MCAS.

a. Applicable Diagnostic Criteria

Mast cells are components of the immune system that typically come to clinical attention in the context of allergic reactions. This can include common conditions such as allergic rhinitis or more extreme manifestations such as anaphylaxis. (Cem Akin, *Mast Cell Activation Syndromes*, 140 J ALLERGY CLIN IMMUNOL 349, 349 (2017) (Ex. 29, p. 1); Cem Akin, Peter Valent & Dean D. Metcalfe, *Mast Cell Activation Syndrome: Proposed Diagnostic Criteria: Towards a Global Classification for Mast Cell Disorders*, 126 J ALLERGY CLIN IMMUNOL 1099 (2010) (Ex. 30; Ex. F).) There are disorders known to relate to primary mast cell defects, such as mastocytosis. (Akin, Valent & Metcalfe, *supra*, at Ex. 30, p. 3.) However, mast cells are also implicated in conditions that result from secondary activation of mast cells resulting from extrinsic mechanisms. (*Id*. at 4.) Some level of mast cell activation is physiologic; however, mast cell activation becomes pathologic in two ways – either through abnormal production or by disproportionate response to stimuli. (Akin, *supra*, at Ex. 29, p. 1.) Mast cell activation can be local or systemic. (*Id*.) "Mast Cell Activation Syndrome" or "MCAS" is a term used to designate "a severe constellation of symptoms within the broader group of disorders of mast cell activation." (*Id*.) MCAS effectively constitutes a clinical presentation that appears like a mast cell disorder, but where the etiology remains idiopathic after known primary and secondary mast cell disorders have been ruled out. (Akin, Valent & Metcalfe, *supra*, at Ex. 30, p. 5.)

There does not appear to be any meaningful dispute between the parties' respective experts regarding the applicable diagnostic criteria for MCAS. Dr. Bernstein discussed R.M.'s case in the context of proposed diagnostic criteria, which I will refer to as the Akin criteria, presented in 2010 in the Journal of Allergy and Clinical Immunology. (Akin, Valent & Metcalfe, *supra*, at Ex. 30.) Respondent's expert, Dr. MacGinnitie, likewise cited these diagnostic criteria and largely discussed R.M.'s presentation in that context. (Ex. C, pp. 4-5.) Although Dr. MacGinnitie also cited more recent papers by Valent et al.,[18] with specific regard to the correct interpretation of urinary markers, he did not otherwise criticize these Akin diagnostic criteria nor propose that any other criteria should be preferred on the whole. The Akin diagnostic criteria require the following:

[18] Peter Valent et al., *Letter to the Editor: Mast Cell Activation Syndrome: Importance of Consensus Criteria and Call for Research*, 142 J. ALLERGY CLIN IMMUNOL P1008 (2018) (Ex. E); Peter Valent et al., *Definitions, Criteria and Global Classification of Mast Cell Disorders with Special Reference to Mast Cell Activation Syndromes: A Consensus Proposal*, 157 INT ARCH ALLERGY IMMUNOL 215 (2012) (Ex. G).

1) Episodic symptoms consistent with mast cell mediator release affecting two or more organ systems evidenced as follows:
    a. Skin: urticaria, angioedema, flushing
    b. Gastrointestinal: nausea, vomiting, diarrhea, abdominal cramping
    c. Cardiovascular: hypotensive syncope or near syncope, tachycardia
    d. Respiratory: wheezing
    e. Naso-ocular: conjunctival injection, pruritus, nasal stuffiness.

2) A decrease in the frequency or severity or resolution of symptoms with antimediator therapy: H_1- and H_2-histamine receptor inverse agonists, antileukotriene medications (cysteinyl leukotrience receptor blockers or 5-lipoxygenase inhibitor), or mast cell stabilizers (cromolyn sodium).

3) Evidence of an increase in a validated urinary or serum marker of mast cell activation: documentation of an increase of the marker to greater than the patient's baseline value during a symptomatic period on ≥2 occasions or, if baseline tryptase levels are persistently >15 ng, documentation of an increase of the tryptase level above baseline value on 1 occasion. Total serum tryptase level is recommended as the marker of choice: less specific (also from basophils) are 24-hour urine histamine metabolites or PGD_2 or its metabolite 11-β prostaglandin F_2.

4) Rule out primary and secondary causes of mast cell activation and well-defined clinical idiopathic entities[19] in Table I.

(Akin, Valent & Metcalfe, *supra*, at Ex. F, p. 3, Ex. 30, p. 12.)

b. Application of the Diagnostic Criteria by the Experts

While the experts largely agree on the correct diagnostic criteria, they differ in their application of that criteria to R.M.'s case. Dr. Bernstein opines that R.M. meets all four of the above criteria while Dr. MacGinnitie disagrees. Specifically, Dr. MacGinnitie raises issues relative to the first and third criteria listed above – multisystem episodic symptoms and urinary markers of mass cell activation. Dr. MacGinnitie also stressed the concern that MCAS is over diagnosed. On the whole, I find Dr. MacGinnitie's opinion more persuasive.

[19] Although Drs. Bernstein and MacGinnitie both copied "Table II" from their respective copies of the 2010 Akin, Valent & Metcalfe article, they are not exactly the same. Dr. Bernstein provided an author manuscript of the paper. (Ex. 30.) Within his copy of the paper, Table II, item 4, indicates "primary (clonal) and secondary disorders of mast cell activation ruled out (Table I)" and does not require ruling out well-defined clinical idiopathic entities. (*Id*. at 12.)

i. Limitations of the Applicable Diagnostic Criteria

As a threshold question, Dr. MacGinnitie is persuasive in suggesting that there is concern in the relevant medical community that MCAS should not be over-diagnosed. (Ex. C, p. 4 (citing Peter Valent et al., *Mast Cell Activation Syndrome: Importance of Consensus Criteria and Call for Research*, 142 J ALLERGY CLIN IMMUNOL 1008 (2018) (Ex. E)).) In that regard, Valent et al., stated that "the diagnosis of MCAS is being applied currently to patients with unresolved complex medical problems after extensive medical evaluations, and a substantial number of these patients do not meet the diagnostic criteria for MCAS." (Valent et al., *supra*, at Ex. E, p. 1.) Important to this point, the Akin criteria relied upon by the experts in this case were establishing novel diagnostic criteria based on tested clinical observations. (Akin, Valent & Metcalfe, *supra*, at Ex. F.) Upon review of the medical literature submitted in this case, it appears that MCAS had not previously been a well-established diagnosis. Indeed, as of 2010, Akin and Valent acknowledged that "'MCAS' as a distinct clinical entity has not been generally accepted nor do there exist definitive criteria for diagnosis." (Akin, Valent & Metcalfe, *supra*, at Ex. 30, p. 1.)

To deter against over-diagnosing, Valent et al., suggested that "MCAS should not be applied on the basis of persistently elevated basal serum tryptase level and not based on the fact that the condition has resisted previous attempts to establish medical diagnosis," and application of the consensus criteria should be cautious. (Valent et al., *supra*, at Ex. E, p. 2.) Akin et al. likewise emphasized that isolated findings relative to only some of the criteria is not sufficient and thus, only complete satisfaction of the criteria supports the diagnosis. (Akin, Valent & Metcalfe, *supra*, at Ex. F, p. 4; Peter Valent et al., *Definitions, Criteria and Global Classification of Mast Cell Disorders with Special Reference to Mast Cell Activation Syndromes: A Consensus Proposal*, 157 INT ARCH ALLERGY IMMUNOL 215 (2012) (Ex. G).) Notably, the literature filed by petitioner cautions:

> In clinical practice some patients with a variety of multisystem symptoms who do not have an identifiable central cause for their complaints are referred for investigation of mast cell activation syndrome. These symptoms can include chronic fatigue; intolerances to various environmental factors, foods, and medications; and neuropsychiatric findings, including memory problems and headaches. These complaints can be present on a chronic basis without well-defined attacks or episodes of mast cell activation. Currently, there is no evidence to suggest that an abnormal mast cell phenotype that results in ongoing chronic mediator release is responsible for these symptoms.

(Akin, *supra*, at Ex. 29, p. 6.)

Accordingly, it does not appear on this record that diagnosis of MCAS based on only partial satisfaction of the Akin criteria would be consistent with generally accepted medicine. *Terran v. Sec'y of Health & Human Servs.*, 195 F.3d 1302 (Fed. Cir. 1999) (holding that in evaluating the reliability of a causation-in-fact theory, it is appropriate for

a special master to utilize the factors set for in *Daubert v. Merrell Dow Pharmaceuticals, Inc*., 509 U.S. 579 (1993)). Although MCAS is a diagnosis of exclusion to some degree, to the extent Dr. Bernstein would lean on the lack of any other viable diagnosis as a substitute for a lack of evidence supporting an MCAS diagnosis (Ex. 27, p. 2), this would not be supported by the consensus of the relevant medical community. (Akin, *supra*, at Ex. 29, p. 6; Valent et al., *supra*, at Ex. E, p. 2; Akin, Valent & Metcalfe, *supra*, at Ex. F, p. 4; Valent et al., *supra*, at Ex. G, p. 8.) Absent consistency with the specific Akin criteria, R.M.'s overall condition otherwise eludes any consistently applied unifying diagnosis, though many of her symptoms have been variously attributed to other conditions, including the somatoform disorder favored by respondent.

ii. Presence of Episodic Symptoms Affecting Two or More Organ Systems

With regard to the first diagnostic criterion, Dr. Bernstein opined that MCAS is the correct diagnosis in light of R.M.'s episodic flushing, nausea, diarrhea, and abdominal cramping. (ECF No. 41, p. 25.) A review of the records supports that R.M. experienced episodic flushing, nausea, and diarrhea and Dr. MacGinnitie agrees. (*See e.g.*, Ex. 3, pp. 88-89; Ex. 6, p. 1; Ex. 20, p. 21; Ex. C., p. 4.) However, Dr. MacGinnitie disagrees that petitioner's reported abdominal pain, her primary complaint, is consistent with the episodic gastrointestinal symptoms such as cramping that meet the diagnostic criteria. Consistent with Dr. MacGinnitie's opinion, a working group recommendation regarding diagnosis and treatment of MCAS filed by petitioner likewise specifically states that "some signs or symptoms that can occur with MCAS do not support this diagnosis when they occur in isolation, such as abdominal pain and diarrhea or flushing, or when they are chronic rather than episodic." (Catherine R. Weiler et al., *AAAAI Mast Cell Disorders Committee Work Group Report: Mast Cell Activation Syndrome (MCAS) Diagnosis and Management*, 144 J ALLERGY CLIN IMMUNOL 883 (2019) (Ex. 38, p. 3).)

Upon my review, the record does not support by preponderant evidence that R.M.'s gastrointestinal symptoms as a whole were episodic in nature as required by the diagnostic criteria. Instead, R.M.'s abdominal or gastrointestinal pain was ongoing and reportedly occurring daily. (*See e.g.*, Ex. 3, pp. 85, 111.) In fact, many of R.M.'s treating physicians refer to the pain as chronic and did not describe any lapses of pain. (*See e.g.*, Ex. 3, p. 28; Ex. 12, p. 62; Ex. 20, p. 11.) During various visits to the emergency room, R.M.'s abdominal pain was identified as persistent and ongoing. (*See e.g.*, Ex. 3, pp. 91, 95.) Dr. Lyon concluded that R.M. had chronic abdominal pain. (Ex. 3, pp. 28-30.) Dr. Singer, during the initial March 10, 2016 evaluation, noted that R.M.'s abdominal pain persisted since onset and the pain was constant, nonstop, and daily. (Ex. 3, pp. 111-12.) In one instance R.M. is directly quoted in the medical record as stating that her stomach pain "never goes away." (Ex. 8, p. 1.) Overwhelmingly, the majority of the records from multiple different physicians support R.M. experiencing continuing, persistent abdominal pain rather than episodes of abdominal pain. Additionally, petitioner, in her affidavit, describes the abdominal pain as constant since the vaccination. (Ex. 1, p. 1.) In her motion, petitioner argued that the day following

vaccination, R.M. experienced severe abdominal pain and the abdominal pain "has been a constant in her life since the vaccination." (ECF No. 41, p. 2.)

Some notations in the medical records suggest that symptoms waxed and waned and some can be interpreted as indicating symptoms were not continuous. (*See e.g.*, Ex. 3, p. 32; Ex. 5, p. 87.) Notably, however, although waxing and waning suggests a fluctuating course, it does not necessarily imply a complete remittance of symptoms. In any event, despite the presence of some contradictory notations, the record as a whole is more consistent with the presence of persistent abdominal pain.[20] Additionally, although R.M.'s diarrhea and nausea were not consistently present, her chronic abdominal pain was consistently treated by her physicians as a relevant and primary gastrointestinal symptom and was factored into preliminary diagnoses such as irritable bowel syndrome or functional abdominal pain. (Ex. 3, pp. 30-31, 35, 115-116.) Moreover, although diarrhea is often cited in the literature as a specific relevant symptom of MCAS, nothing in the literature filed in this case suggests that it should be viewed in isolation where the overall gastrointestinal presentation is not episodic.

A further consideration is that the episodic multisystem presentation seen in MCAS is itself evidence of an anaphylactic-type mast cell activation event. (AAAAI Work Group, *supra*, at Ex. 38, p. 3.) For this reason, the symptoms associated with the two differing organ systems more strongly suggest MCAS when they occur concurrently. (*Id*.) R.M.'s medical records do not reflect that her diarrhea and flushing/urticaria occurred concurrently (*see e.g.*, Ex. 8, pp. 1-4; Ex. 20, pp. 21, 53, 66) and diarrhea is otherwise a relatively non-specific symptom. Additionally, some of the literature filed in this case has cautioned that gastrointestinal diseases can be confused for mass cell activation. (Valent et al., *supra*, at Ex. G, p. 8.) (As just one example, irritable bowel syndrome can also have a fluctuating course.) Thus, even isolating her symptom of diarrhea from her overall gastrointestinal presentation, it remains difficult to connect that gastrointestinal symptom to her flushing as evidence of an episodic MCAS presentation.

On the whole, the record provides little basis for considering R.M.'s gastrointestinal symptoms separately. Moreover, R.M.'s gastrointestinal symptoms were persistent rather than episodic and therefore inconsistent with the diagnostic

[20] The process for making determinations in Vaccine Program cases regarding factual issues begins with consideration of the medical records. 42 U.S.C. § 300aa-11(c)(2). The special master is required to consider "all [ ] relevant medical and scientific evidence contained in the record," including "any diagnosis, conclusion, medical judgment, or autopsy or coroner's report which is contained in the record regarding the nature, causation, and aggravation of the petitioner's illness, disability, injury, condition, or death," as well as "the results of any diagnostic or evaluative test which are contained in the record and the summaries and conclusions." 42 U.S.C. § 300aa-13(b)(1). The special master shall determine whether compensation is appropriate based "on the record as a whole." 42 U.S.C. § 300aa-13(a)(1); *See also Gamache v. Sec'y of Health & Human Servs.*, 27 Fed. Cl. 639 (1993), *aff'd*, 5 F.3d 1505 (Fed. Cir. 1993) (finding that the special master did not commit reversible error because pursuant to the Vaccine Act, "the special master must make the determination 'on the record as a whole' as to whether petitioner has established the pertinent matters by a preponderance of the evidence.").

criteria for MCAS.[21] (Akin, Valent & Metcalfe, *supra*, at Ex. 30; AAAAI Work Group, *supra*, at Ex. 38, p. 3.)

Petitioner also argued that R.M. suffered from episodic symptoms affecting her cardiovascular system including tachycardia, POTS (tilt table). (ECF No. 41, pp. 22, 25.) Dr. Bernstein did not address this issue specifically, but did state that "there are now many reports of MCAS overlapping with dysautonomia which could explain many of [R.M.'s] other atypical symptoms." (Ex. 37, p. 2.) Petitioner also filed an article by Taylor A. Doherty and Andrew A. White, positing that POTS is associated with mast cell activation. (Taylor A. Doherty & Andrew A. White, *Postural Orthostatic Tachycardia Syndrome and the Potential Role of Mast Cell Activation*, 215 AUTONOMIC NEUROSCIENCE BASIC CLIN 83 (2018) (Ex. 39).) They reported a study of 177 POTS patients that found eight females that met both the criteria for POTS and MCAS, five had orthostatic hypotension and MCAS, and 16 had POTS and flushing. (Doherty & White, *supra*, at Ex. 39, p. 2.) However, the study was in 2005. (*Id*.) The subsequently created Akin diagnostic criteria and working group recommendations do not support POTS or dysautonomia as diagnostic of MCAS. (Akin, Valent & Metcalfe, *supra*, at Ex. F.) In fact, in setting forth the proposed diagnostic criteria, Akin specifically addressed this possible association and concluded that additional research would be necessary to link POTS to mast cell activation, noting that dysautonomia itself remains a relevant pathologic process. (Akin, *supra*, at Ex. 29, p. 6.) Therefore, even if the possible association highlighted by petitioner helped to explain additional otherwise atypical symptoms R.M. experienced, neither the presence of POTS nor dysautonomia would substitute for the requisite episodic multisystem presentation or otherwise contribute to her diagnostic picture in the first instance.

Although he discussed R.M.'s overall clinical picture broadly, Dr. Bernstein has not otherwise specifically pointed to any additional symptoms that would contribute to the multisystem presentation required by the diagnostic criteria. Apart from discussing abdominal pain and dysautonomia, he only indicated generally that "[m]ast cell activation symptoms can involve essentially any organ system . . ." (Ex. 37, p. 2.)

For all of these reasons, Dr. MacGinnitie is persuasive in explaining that R.M.'s presentation was not consistent with episodic symptoms affecting two or more organ systems as described by the Akin diagnostic criteria. Accordingly, petitioner has not presented preponderant evidence that R.M. meets this first diagnostic criterion.

[21] I do note that prior to her vaccination, R.M. did have several isolated episodes of gastrointestinal complaint. In one instance, this was in association with an illness inclusive of fever and sore throat. (Ex. 26, p. 20.) In several other instances this was related to constipation. (Ex. 26, pp. 14-17.) Constipation itself does not support a diagnosis of MCAS (AAAAI Working Group, *supra*, at Ex. 38, p. 3); however, taking these complaints at face value could raise the question of whether R.M.'s post-vaccination gastrointestinal complaints represented one extended episode in an otherwise pre-existing MCAS. Notably, however, although Dr. Bernstein highlights the existence of these prior complaints, his opinion is based on the premise that what R.M. experienced post-vaccination remained recurrent or episodic. (Ex. 27, p. 1; Ex. 37, p. 2.) Moreover, Dr. MacGinnitie opined that the persistence of R.M.'s post-vaccination abdominal complaints is inconsistent with MCAS. (Ex. C, p. 4.) Nothing in Dr. Bernstein's reports would contradict that opinion.

iii. Urinary Markers

The second significant issue raised by Dr. MacGinnitie relates to the third diagnostic criterion. Because MCAS is a syndrome based largely on heterogeneous clinical presentation, the ability to confirm mast cell activation by laboratory test is important. Valent et al., explain that "[t]his requirement for biochemical evidence of mast cell activation is of importance in order to avoid applying the term MCAS to a diagnosis of a disorder unrelated to mast call pathology but presenting with similar symptoms in the absence of biochemical proof of mast cell activation." (Akin, Valent & Metcalfe, *supra*, at Ex. 30, p. 5.) "Documentation of mast cell mediator release associated with symptomatic episodes provides critical information to support the premise that symptoms are due to mast cell activation." (*Id*. at 6.)

As explained above, the Akin diagnostic criteria suggest several methods of detecting mast cell activation from either urine or serum. The strongest evidence – the "marker of choice" – is total serum tryptase. (Akin, Valent & Metcalfe, *supra*. at Ex. 30, p. 12 (Table II); Akin, *supra*, at Ex. 29, p. 3.) In R.M.'s case, she was tested for tryptase by both the Mayo Clinic and Dr. Doshi and the results were normal. (Ex. 12, p. 14; Ex. 6, p. 12.) Elevated tryptase was never documented.[22]

Nonetheless, according to Akin, a less specific finding still potentially supportive of MCAS is elevated urine histamine metabolites. (Akin, *supra*, at Ex. 29, p. 5.) Specifically:

> Prostaglandin D_2 is a known marker of mast cell activation. Its metabolite 11-β-prostaglandin $F_2\alpha$ can be measured in urine as a marker of mast cell activation. However, this mediator is not specific for mast cell activation. A number of immune cells, including eosinophils, and nonimmune cells are capable of producing prostaglandin D_2 through 2 structurally different enzymatic pathways. Therefore it is not recommended to rely solely on a single measurement of an increased prostaglandin D_2 or $F_2\alpha$ level as a marker of mast cell activation unless one of the other markers are also present in the patient.

(*Id*. at 2.)

[22] Petitioner highlights the fleeting nature of these findings, noting that "[t]his is a difficult disease to catch in the act." (ECF No. 44, pp. 3-4.) Notably, R.M.'s physicians were aware of this difficulty, indicating that "[s]hould her random sample from urine mast cell mediators return negative, I would recommend repeating a collection with a void after her next episode of facial flushing, abdominal cramping, and diarrhea, as testing in the absence of symptoms is often negative." (Ex. 12, p. 23.) This tempers the weight and significance of this lack of confirmatory tryptase finding; however, the lack of confirmation still fails to provide any affirmative evidence supporting petitioner's claim and remains a factor under the relevant diagnostic criteria. Despite the apparent difficulty in obtaining positive test results, the literature explains that elevated tryptase is still the preferred diagnostic marker.

Akin further cautions that "urinary histamine levels can be influenced by bacterial flora of the urinary tract, storage condition, and diet." (*Id*.) Petitioner is correct that Akin indicated that "[t]wenty-four hour samples are recommended, although shorter collection times or spot analysis are also acceptable." (*Id*.) Critically, however, respondent is also correct in noting that the diagnostic criteria require elevated urine metabolites on at least two occasions. (Akin, Valent & Metcalfe, *supra*, at Ex. 30, p. 12 (Table II).)

Subsequently, Akin, Valent, and others wrote in 2018 that:

> Currently, only a few biomarkers are recognized as implicating [mast cell] activation in pathology. One example is histamine or its metabolites when measured in urine, although histamine is produced by [mast cell]s and basophils. Measurement of tryptase levels in bodily fluids is more specific and generally considered the most reliable diagnostic test of [mast cell] involvement and thus strongly recommended within consensus diagnostic criteria. Prostaglandin D2 and histamine metabolite levels in urine can both increase over baseline values in patients with MCAS and have also been measured and used as a guide for treatment, although their increase might not always be associated with [mast cell] activation.

(Valent et al., *supra*, at Ex. E, p. 2.)

In R.M.'s case, the Mayo Clinic identified elevated 2,3-dinor 11b Prostaglandin F2a of 8,447 against a reference range of up to 5,205 based on a random (i.e. not 24-hour) sample collection. (Ex. 12, p. 14.) However, N-Methylhistamine was normal. (*Id*.) This single elevated Prostaglandin F2a finding is the only laboratory result identified by petitioner, Dr. Doshi, or Dr. Bernstein, as supportive of an MCAS diagnosis. (ECF No. 41, p. 24; Ex. 6, p. 3; Ex. 27, p. 2.) In that regard, Dr. Bernstein stresses that "the Mayo clinic laboratory is one of the few laboratories in the US that has a reliable assay for this marker." (Ex. 27, p. 2.) Importantly, however, in R.M.'s own report the laboratory cautions that the reference value for this test has not been established for patients less than 18 years of age, a group that would include R.M. (Ex. 12, p. 6.) Pertinent to this point, respondent stresses that no baseline value is otherwise available for R.M. (ECF No. 42, pp. 12-13.)

Dr. MacGinnitie contends that current recommendations are that "only tryptase, a more direct measure of mast cell activation be used as a diagnostic criterium." (Ex. C, p. 5 (citing Akin, Valent & Metcalfe, *supra*, at Ex. E; Valent et al., *supra*, at Ex. G).) Dr. MacGinnitie further contends that urine histamines "must be measured over a 24-hour sample and on 2 or more occasions to be meaningful." (Ex. C, p. 6.) To the extent Dr. MacGinnitie would seek to categorically exclude urine metabolites from the diagnostic criteria or limit their consideration only to 24-hour samples, he is not persuasive. In light of all of the above, however, he is persuasive in explaining that this isolated finding of urine metabolites in a single random sample is not meaningful evidence of mast cell activation. Although Dr. Bernstein specifically addressed the issue of a random sample versus a 24-hour sample, he did not otherwise substantiate his reliance on a single

finding of elevated urine metabolites in the face of otherwise normal lab results and the medical literature filed by petitioner does not support that reliance.[23] (Ex. 37, p. 2.)

For all of these reasons, petitioner has not presented preponderant evidence that R.M.'s presentation meets the third diagnostic criteria for MCAS, requiring evidence of an increase in a validated urinary or serum marker of mast cell activation.

iv. Relief on H1, H2, Cromolyn Treatment

The issues identified above regarding symptom presentation and the lack of biochemical confirmation are fatal to Dr. Bernstein's application of the Akin diagnostic criteria. In the interest of completeness, however, I do note that it is undisputed that R.M. improved with cromolyn and ketotifen treatment. (Ex. C, p. 6.) Dr. MacGinnitie did suggest, however, that R.M.'s prior treatment with antihistamines leaves this criterion difficult to interpret. (*Id*.) In any event, the literature in this case explains that "response to anti-mediator therapy, while a diagnostic requirement, cannot be used alone. For instance, gastrointestinal mast cells degranulate in association with a number of disorders; and antihistamines, cromolyn, and leukotriene antagonists, if effective, do not necessarily implicate mast cells." (Akin, Valent & Metcalfe, *supra*, at Ex. 30, pp. 5-6.)

c. Treating Physician Opinion(s)

In addition to the expert assessments, it is also important to look to the opinions of R.M.'s treating physicians. Medical records and/or statements of a treating physician's views do not *per se* bind the special master to adopt the conclusions of such an individual, but they must be considered and carefully evaluated. *See* Section

[23] More recently, the working group report also explained that:

> Once released, histamine is metabolized rapidly (half-life, 1-2 minutes), primarily to N-methylhistamine. Several investigations of urinary histamine metabolites have demonstrated clear utility to aid in the evaluation and diagnosis of [systemic mastocytosis] . . . However, for investigating MCAS, measurement of urine N-methylhistamine levels has demonstrated little clinical utility, perhaps because metabolites generated just after [mast cell] activation were not collected. However, it can be supportive if increased levels are found in conjunction with other mediators, such as PGD2 metabolites, even though cell source might be ambiguous. Further studies are needed to evaluate how measurement of urine N-methylhistamine levels might be optimally used for the evaluation and management of MCAS.

(AAAAI Working Group, *supra*, at Ex. 38, p. 4.) In R.M.'s case, Prostaglandin was elevated but N-methylhistamine was not. Although Dr. MacGinnitie did highlight the normal N-methylhistamine finding, nothing in the record directly discusses whether the normal N-methylhistamine confounds the finding of elevated Prostaglandin. This passage seems to suggest that the potential diagnostic utility of R.M.'s elevated Prostaglandin F2a exists in its ability to confirm elevated N-methylhistamine. This may raise a further question as to the value of this finding. However, it is not ultimately necessary to explore that question because, even accepting the elevated Prostaglandin F2a as a genuine finding, the medical literature makes clear that elevated Prostaglandin F2a is a non-specific finding that does not lead to a diagnosis of MCAS in isolation.

13(b)(1) (providing that "[a]ny such diagnosis, conclusion, judgment, test result, report, or summary shall not be binding on the special master or court"); *Snyder v. Sec'y of Health & Human Servs.*, 88 Fed. Cl. 706, 746 n.67 (2009) ("there is nothing ... that mandates that the testimony of a treating physician is sacrosanct—that it must be accepted in its entirety and cannot be rebutted").

As with expert testimony offered to establish a theory of causation, the opinions or diagnoses of treating physicians are only as trustworthy as the reasonableness of their suppositions or bases. The views of treating physicians should also be weighed against other, contrary evidence also present in the record—including conflicting opinions among such individuals. *Hibbard v. Sec'y of Health & Human Servs.*, 100 Fed. Cl. 742, 749 (2011) (not arbitrary or capricious for special master to weigh competing treating physicians' conclusions against each other), *aff'd*, 698 F.3d 1355 (Fed. Cir. 2012); *Caves v. Sec'y of Health & Human Servs.*, 100 Fed. Cl. 119, 136 (2011), *aff'd*, 463 Fed. Appx. 932 (Fed. Cir. 2012); *Veryzer v. Sec'y of Health & Human Servs.*, No. 06–522V, 2011 WL 1935813, at *17 (Fed. Cl. Spec. Mstr. Apr. 29, 2011), *mot. for review den'd*, 100 Fed. Cl. 344, 356 (2011), *aff'd without opinion*, 475 Fed. Appx. 765 (Fed. Cir. 2012).

In this case, I am not persuaded that R.M.'s medical records, and the opinions of her treating physicians, provide preponderant evidence that she suffered MCAS when viewed as a whole. R.M. was evaluated by a number of specialists, including at a pediatric gastroenterology clinic (CNP Zeng-Wang (Ex. 21, pp. 432-35)), and by three pediatric neurologists (Drs. Allarakhia (Ex. 3, p. 91), Knierbein (Ex. 20, pp. 98-102), and McCormick (Ex. 8, pp. 11-14)), a pediatric endocrinologist (Dr. Menon (Ex. 20, pp. 88-92)) and two rheumatologists (Dr. Sura (Ex. 20, pp. 108-12) and CNP Patty-Resk (Ex. 21, pp. 4-10)). Although no other unifying diagnosis was reached, none of these specialists diagnosed or suspected MCAS or felt a referral to an allergist was indicated. R.M. also underwent two very thorough multidisciplinary evaluations of her condition, neither of which resulted in a diagnosis of MCAS. First, she was hospitalized in April of 2016 at the University of Michigan hospital where she was assessed as having a somatoform disorder. (Ex. 20, pp. 215-19.) Later, she was extensively evaluated at the Mayo Clinic. (Ex. 12.) At the Mayo Clinic the possibility of MCAS was specifically considered along with a number of other possible conditions. Ultimately, however, the Mayo Clinic team never moved beyond suspicion to diagnosis. Instead, they recommended further follow up with an allergist. (Ex. 12, p. 14.)

Petitioner stresses the specific notation by Dr. Klaas that resulted in the referral to an allergist, stating:

> In this case, Dr. MacGinnitie's opinion simply does not align with Dr. Klaas' comment that "We had briefly discussed mast cell problems (a type of allergic cell), which can cause flushing and abdominal pain and diarrhea. [R.M.]'s level is elevated. As a result, I'd like for her to be seen by an Allergist when she returns this summer to see Dr. Mardini." Ex. 12, p. 14. Dr. Klaas is the treater. He saw R.M. directly and evaluated her. Dr. Doshi

> then agreed that she has Mast Cell Activation Disorder. Ex. 5, p. 4. Respondent cannot easily sweep these treating physician opinions and diagnoses under the rug as though they do not matter or are simply "mistakes" that suit Respondent's position.

(ECF No. 44, p. 3 (footnote omitted).) Petitioner contends that Dr. Klaas's statement constitutes a diagnosis in the first instance later ratified R.M.'s allergist, Dr. Doshi. I disagree. First, Dr. Klaas clearly couched her statement in tentative terms. She noted the ability of the condition to cause the relevant symptoms of flushing and abdominal pain, but with regard to R.M.'s own condition only stated that R.M.'s single marker of the condition was elevated. She did not actually state that R.M. had MCAS. Additionally, in follow up communication contained in the same record, Dr. Klaas further states that "[t]he next step is to meet with an allergist to see if a medication may help to control symptoms." (Ex. 12, p. 14.) As explained above, response to treatment is a required diagnostic criterion. It is not reasonable to speculate that Dr. Klaas would render a MCAS diagnosis by referencing this diagnostic consideration as a necessary next step without appreciating its place in the relevant diagnostic criteria. Accordingly, although she clearly *suspected* MCAS, Dr. Klaas did not, and could not, diagnose R.M. as having MCAS at that time. Her record is better understood as one recommending further diagnostic evaluation and not simply treatment for an established diagnosis.

As noted above, the allergist that R.M.'s family ultimately chose to consult based on Dr. Klaas's recommendation was Dr. Doshi. He is the only physician in R.M.'s entire medical history to have diagnosed R.M. with MCAS.[24] However, his diagnosis suffers several significant shortcomings.

First, Dr. Doshi misidentified R.M.'s urinalysis as a 24-hour result rather than as a single, random sample. (Ex. 6, p. 3.) Although, as described above, a random sample is not wholly without diagnostic value, both the medical literature and expert presentations in this case make clear that a 24-hour urinalysis is preferred and therefore represents *stronger* diagnostic evidence. Accordingly, Dr. Doshi's medical record indicates that his opinion was likely based on a mistaken belief as to the strength of the evidence underlying his diagnosis. This error is especially significant in this particular case because the urinalysis is the one piece of diagnostic evidence that Dr. Doshi explicitly identified during his initial assessment as leaving him "even more inclined" to support a diagnosis of MCAS. (*Id*.) In any event, assuming *arguendo* that Dr. Doshi was aware that the urinalysis was based on a random sample, his reliance on that result still suffers the same limitations as discussed above relative to Dr. Bernstein's application of the MCAS diagnostic criteria.

Apart from his reliance on R.M.'s urinalysis, Dr. Doshi did not otherwise explicitly describe the diagnostic criteria he considered. Dr. Doshi appears to have relied at least

[24] Dr. Fisher later accepted Dr. Doshi's diagnosis without any separate assessment. (Ex. 5, p. 110.) Additionally, Dr. Fatima recorded R.M. as having mast cell disorder based on her history. (Ex. 45, p. 4-7.) The ED treating physician also recorded mast cell disorder based on her history. (Ex. 5, pp. 124-25.)

in part on his review of the Mayo Clinic evaluation, which again, suspected but did not conclude that R.M. had MCAS. In a later follow up, Dr. Doshi did note due to R.M.'s response to medication that "I feel her symptoms most likely fit with a clinical diagnosis of mast cell activation disorder." (Ex. 22, p. 4.) However, as explained above, response to medication represents only one of four required criteria under accepted diagnostic standards and does not itself implicate mast cells.

Additionally, Dr. Doshi does not appear to have accounted for the fact that the confirmatory tests that he himself ordered did not support his initial diagnosis. Although Dr. Doshi charted an MCAS diagnosis at his initial evaluation, he also called for "the parents [to] call the Mayo Clinic to have the biopsies from [R.M.]'s recent EGD and colonoscopy stained for CD119 and CD25 markers, to further confirm a mast cell disorder diagnosis." (Ex. 6, p. 3.) Ms. Mulrenin did subsequently request that the requested staining be done (Ex. 12, p. 12) and the Mayo Clinic confirmed that the results were negative (Ex. 12, p. 11). Dr. Doshi also indicated "[f]or further evaluation of the mast cell, I would also like [R.M.] to get blood work done, which will include a chronic uticaria index, total IgE, Thyroid Ab levels, Serum Histamine, Serum Tryptase, and prostaglandins D2 and F2 (if available)." (*Id*.) Yet all of the lab results contained within Dr. Doshi's file appear to be within normal reference ranges. (Ex. 6, pp. 4-16.) Dr. Doshi continued to see R.M. for follow up care on the basis that she had MCAS; however, neither his records nor the Mayo Clinic records indicate that he was made aware of[25] or accounted for the negative biopsy staining nor do Dr. Doshi's records include any discussion of her normal lab results.

In sum, although Dr. Doshi considered R.M. to have MCAS, his view is a minority view among R.M.'s treating physicians. Additionally, his own records suggest reason to doubt the sufficiency of his assessment. Moreover, he did not fully explain the basis for his opinion and Dr. MacGinnitie's persuasive discussion of the Akin diagnostic criteria casts further doubt on that assessment. Accordingly, on balance, the opinions of R.M.'s treating physicians do not support a diagnosis of MCAS.

VI. Petitioner Has Not Met Her Burden of Proof

As explained above, petitioner's burden is to present preponderant evidence supporting the three *Althen* prongs and that analysis is premised on petitioner's ability to establish the fact of R.M.'s alleged injury. Because none of R.M.'s treating physicians ever opined that her clinical course was vaccine-related, and because her expert, Dr. Bernstein, premised his causal opinion exclusively on the presence of MCAS, my conclusion that R.M. did not suffer MCAS necessarily means petitioner cannot meet her burden of proof. Nonetheless, I will briefly address several reasons why petitioner's claim would fail the *Althen* test even assuming *arguendo* that R.M. did have MCAS.

[25] The Mayo Clinic records indicate that Dr. Tung relayed the staining results to Ms. Mulrenin and indicated that she should contact his secretary if she wished for them to be provided directly to R.M.'s allergist. (Ex. 12, p. 11.) There is no indication of any further follow up in the Mayo Clinic records, the biopsy staining results do not appear anywhere in Dr. Doshi's records, and no notation was made to suggest that Ms. Mulrenin reported the results orally.

a. *Althen* prong one

Under *Althen* prong one, petitioner must provide a "reputable medical theory," demonstrating that the vaccine received can cause the type of injury alleged. *Pafford v. Sec'y of Health & Human Servs.*, 451 F.3d 1352, 1355–56 (Fed. Cir. 2006) (citations omitted). However, to satisfy this prong, petitioner's theory must be based on a "sound and reliable medical or scientific explanation." *Knudsen*, 35 F.3d at 548; *Boatmon*, 941 F.3d at 1359. Petitioner has not presented a sound and reliable theory by preponderant evidence.

Importantly, there are significant limitations in our understanding of MCAS. As explained above, MCAS is a relatively novel diagnosis that exists within a spectrum of mast cell disorders. In order to reach a diagnosis of MCAS, primary and secondary mast cell disorders must be eliminated. (Akin, Valent & Metcalfe, *supra*, at Ex. 30.) In the absence of such a disorder, the etiology of MCAS is largely discussed by the literature as remaining idiopathic. (Akin, *supra*, at Ex. 29, p. 3.) It is not even understood whether mast cells act as the pathogenic component of mast cell disorders or whether they are a response to another pathological process. (*Id*. at 1.) Some idiopathic events may be explained by basophils rather than mast cells. (Akin, Valent & Metcalfe, *supra*, at Ex. 30, p. 5.)

Even reducing the causal theory to one of a trigger, the relationship between MCAS and triggering events remains inconclusive. Nothing in the diagnostic criteria suggests that recurrent episodes must be linked to a triggering event. For example, the literature explains that "[i]f use of such a pharmacologic agent is associated with all episodes under question, the diagnosis then is one of an adverse reaction to a drug, not MCAS. However, if the administration of such an agent does not always precede an episode, then the patient could also have MCAS." (*Id*.) Moreover, none of the literature filed in this case discussed vaccines as a possible trigger of MCAS. According to the literature filed in this case, "[r]eported triggers or potentiating factors can include hot water, alcohol, drugs, stress, exercise, hormonal fluctuations, infection, and/or physical stimuli, such as pressure or friction. A connection between such triggers and [mast cell] activation is generally inconclusive, except in patient with rare monogenic disorders." (AAAAI Working Group, *supra*, at Ex. 38, p. 3.) Relatedly, even if a specific trigger such as a vaccine could be implicated in a single symptom episode, nothing in the literature supports the idea that an isolated trigger can explain an entire, progressive clinical course of the type Dr. Bernstein identifies in this case.

In his first report, Dr. Bernstein sought to link vaccines to allergic disease and mast cell production generally. (Ex. 27, p. 2.) Setting aside the merits of his specific citations (Dr. MacGinnitie challenges the credibility of one publication), for the reasons indicated above, he is not persuasive in closing the gap between immune reactions generally and the specific, expected clinical presentation of MCAS. In his second report, Dr. Bernstein further sought to connect R.M.'s clinical course to her vaccination by establishing a connection between the influenza A viral infection and mast cell

activation. However, even if I fully credited the specifics of that connection, it would not in itself establish that vaccination results in a pathologic activation of mast cells. Nothing else in Dr. Bernstein's reports or reliance materials otherwise supports that specific contention. Moreover, this proposed connection does nothing to close the above-discussed gaps in our understanding of MCAS. In any event, Dr. Bernstein's discussion of his own theory is perfunctory, and his opinion is not well explained.

b. *Althen* prong two

The second *Althen* prong requires proof of a logical sequence of cause and effect, usually supported by facts derived from a petitioner's medical records. *Althen*, 418 F.3d at 1278; *Andreu*, 569 F.3d at 1375–77; *Capizzano*, 440 F.3d at 1326; *Grant v. Sec'y of Health & Human Servs.*, 956 F.2d 1144, 1148 (Fed. Cir. 1992). Here, none of R.M.'s physicians opined that her condition was vaccine-caused. In fact, even Dr. Doshi, the only physician to have diagnosed MCAS, recommended that petitioner continue receiving the influenza vaccine. (Ex. 22, p. 5.) If Dr. Doshi felt R.M.'s MCAS was vaccine-related, this would not be consistent with the typical standard of care for MCAS. "General principles of the management of mast cell activation syndromes include avoidance of triggers . . ." (Akin, *supra*, at Ex. 29, p. 4.) Moreover, the above-discussed literature suggests that infection can be a relevant trigger for MCAS. (AAAAI Working Group, *supra*, at Ex. 38, p. 3.) In that regard, at the time of her vaccination, R.M. was experiencing both an upper respiratory infection and severe otitis media. (Ex. 3, pp. 1-3.) In fact, Dr. Bernstein specifically cited both infections as having a causal role along with R.M.'s vaccination. (Ex. 37, p. 3.) Yet, he failed to explain why his novel theory of vaccine-causation is necessary to explain R.M.'s condition when she was also experiencing infection, which is a known trigger of MCAS episodes. In contrast, Dr. MacGinnitie stresses that R.M. tolerated prior flu vaccines well.[26] (Ex. C, pp. 6-7.) Additionally, as explained in the preceding section, there is not preponderant evidence that a single trigger explains an extended clinical course of symptoms.

c. *Althen* prong three

The third *Althen* prong requires establishing a "proximate temporal relationship" between the vaccination and the injury alleged. *Althen*, 418 F.3d at 1281. A petitioner must offer "preponderant proof that the onset of symptoms occurred within a timeframe which, given the medical understanding of the disorder's etiology, it is medically acceptable to infer causation." *de Bazan v. Sec'y of Health & Human Servs.*, 539 F.3d 1347, 1352 (Fed. Cir. 2008). The explanation for what is a medically acceptable timeframe must also coincide with the theory of how the relevant vaccine can cause an injury (*Althen* prong one's requirement). *Id.*; *Shapiro v. Sec'y of Health & Human Servs.*, 101 Fed. Cl. 532, 542 (2011), *recons. den'd after remand*, 105 Fed. Cl. 353 (2012), *aff'd mem.*, 503 Fed. Appx. 952 (Fed. Cir. 2013); *Koehn v. Sec'y of Health &*

[26] Petitioner does stress that the flu vaccine has a different formulation each year. (ECF No. 44, n. 1.) Petitioner also notes that she bears no burden of proof with respect to petitioner's prior vaccinations. (*Id.* at 1-2.) I agree that standing alone R.M.'s ability to tolerate prior flu vaccinations would not be dispositive; however, that does not render her vaccination history irrelevant.

Human Servs., No. 11–355V, 2013 WL 3214877, at *26 (Fed. Cl. Spec. Mstr. May 30, 2013), *mot. for review den'd*, (Fed. Cl. 2013), *aff'd*, 773 F.3d 1239 (Fed. Cir. 2014).

Petitioner argues that "[r]egardless of whether the onset was in November of 2015 or December of 2015, the onset of her symptoms within days to a few weeks post-vaccination falls well within the Vaccine Program case precedent for the onset of immune-mediated illness post-vaccination." (ECF No. 41, p. 29.) This is not adequate. Petitioner's medical theory is not as broad as any "immune-mediated" illness. Although Dr. Bernstein proposed specific mechanisms relating to allergic response in form of mast cell activation, he provided no expert assessment of the timing of the temporal relationship at issue. Nor is the literature specifically relating to MCAS illuminating on that point. To the extent MCAS can be equated mechanistically to a mild form of anaphylaxis,[27] such a reaction typically occurs quickly upon exposure. *See e.g.*, 42 C.F.R. §100.3(a) (including anaphylaxis within 4 hours of vaccination as a table injury). MCAS may not occur on the same timescale as anaphylaxis; however, petitioner simply has not substantiated that the relevant timeframe is days to weeks.

VII. Conclusion

Both petitioner and R.M. have my sympathy for the pain and suffering R.M. endured and I do not doubt petitioner's sincerity in bringing this claim. However, for all the reasons discussed above, after weighing the evidence of record within the context of this program, I cannot find by preponderant evidence that R.M. suffered the alleged injury of MCAS and moreover that R.M.'s condition was vaccine-caused. Therefore, this case is dismissed.[28]

IT IS SO ORDERED.

s/Daniel T. Horner
Daniel T. Horner
Special Master

[27] For example, "[a]n extreme form of mast cell activation is anaphylaxis." (Akin, *supra*, at Ex. 29, p. 1.)

[28] In the absence of a timely-filed motion for review of this Decision, the Clerk of the Court shall enter judgment accordingly.